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Complex(kinase/cell division protein)

PDB id: 1ol5

Name: Complex(kinase/cell division protein)

Title: Structure of aurora-a 122-403, phosphorylated on thr287, thr288 and bound to tpx2 1-43

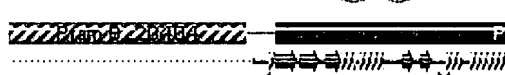
Structure: Serine/threonine kinase 6. **Synonym:** aurora-a, serine/threonine kinase 15, aurora/ipl1-related kinase 1, aurora-related kinase 1, hark1, breast-tumor-amplified kinase. Chain: a. Fragment: catalytic domain residues 122-403. Engineered: yes. Other details: phosphorylated on thr287, thr288. Restricted expression proliferation associated

Source: Homo sapiens. Human. Expressed in: escherichia coli.

Biological unit: Dimer (from PDB file)

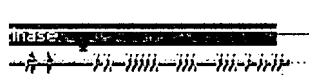
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Seq:



Struc:

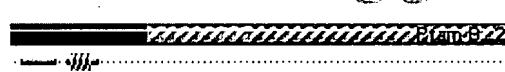
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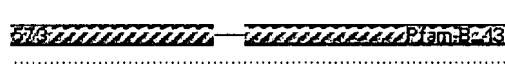
Chain B: Q9ULW0 (TPX2\_HUMAN) [Pfam]

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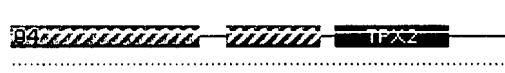
Struc:

Seq:



Struc:

Seq:



Struc:

Biological unit = asymmetric unit,  
as shown  
(as defined in PDB file)



Contents

## Description

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## Protein chains

A 266 a.a. \*

B 30 a.a. \*

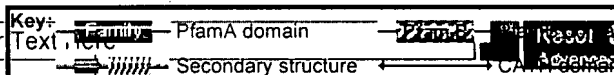
## Ligands



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\* PDB and UniProt seqs differ at 2 residue positions (black crosses)

**Metal ions**

☉ \_MG ×3

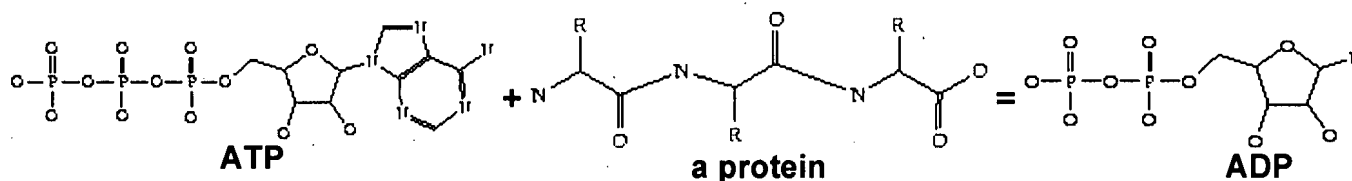
**Waters ×144**

\* Residue conservation analysis

**Tools**[Image Generation](#)[AstexViewer™@MSD-EBI](#)[Run PROCHECK](#)[Clefs Calculation](#)**Enzyme class:** Chain A: [E.C.2.7.1.37](#) [[IntEnz](#)] [[ExPASy](#)] [[KEGG](#)] [[BRENDA](#)]**Reaction:** ATP + a protein = ADP + a phosphoprotein ([see diagram below](#))**Function:** ([see GO annotation below](#))**Resolution:** 2.50Å**R-factor:** 0.194**R-free:** 0.252**Authors:** R.Bayliss, E.Conti**Key ref:** R.Bayliss et al. (2003). Structural basis of Aurora-A activation by TPX2 at the mitotic spindle.. *Mol Cell*, 12, 85-862. [PubMed id: [14580337](#)] [DOI: [10.1016/S1097-2765\(03\)00392-7](#)] ☉**Date:** 06-Aug-03**Release date:** 30-Oct-03**Related entries:** 1muo crystal structure of aurora-2, an oncogenic serine-threonine kinase  
1ol6 structure of unphosphorylated d274n mutant of aurora-a  
1ol7 structure of human aurora-a 122-403 phosphorylated on thr287, thr288**Gene Ontology (GO) functional annotation**

<b>Biological process</b>	protein amino acid phosphorylation	1 term(s)
<b>Biochemical function</b>	protein kinase activity	3 term(s)






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**Enzyme reaction for E.C.2.7.1.37**Molecule diagrams generated from .mol files obtained from the [KEGG ftp site](#).DOI no: [10.1016/S1097-2765\(03\)00392-7](#)  
PubMed id: [14580337](#)**Key ref**  
*Mol Cell* 12:85**Structural basis of Aurora-A activation by TPX2 at the mitotic spindle**

R.Bayliss, T.Sardon, I.Vernos, E.Conti.

**ABSTRACT**

Aurora-A is an oncogenic kinase essential for mitotic spindle assembly. It is activated by phosphorylation and by the microtubule-associated protein TPX2, which also localizes the kinase to spindle microtubules. We have uncovered the

EMBL-EBI  Molecular mechanism of Aurora-A activation by determining crystal structures of its phosphorylated form both with and without the 15-residue long domain of TPX2 that we identified as fully functional for kinase activation and protection.    

dephosphorylation. In the absence of TPX2, the Aurora-A activation segment is in an inactive conformation, with the critical phosphothreonine exposed and accessible for deactivation. Binding of TPX2 triggers no global conformational changes in the kinase but pulls on the activation segment, swinging the phosphothreonine into a buried position and locking the active conformation. The recognition between Aurora-A and TPX2 resembles that between the cAPK catalytic core and its flanking regions, suggesting this molecular mechanism may be a recurring theme in kinase regulation.

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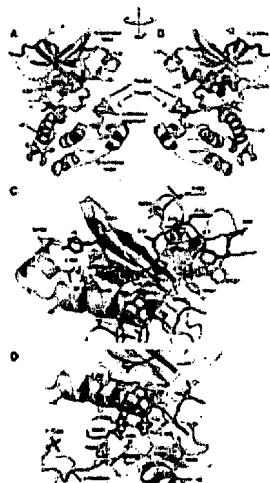


Figure 3.

Figure 3. Structure of Aurora-A Bound to TPX2 (A) View of the complex between the catalytic domain of human Aurora (AuroraΔN, yellow) and the N-terminal domain of TPX2 shown in typical kinase orientation. An upstream stretch of TPX2 (red) binds at the N-terminal lobe of Aurora-A, and a downstream stretch (pink) binds between the two lobes. A dotted line in pink marks the approximate path of the linker connecting the two TPX2 stretches (disordered and not modeled). (B) View of the complex after a 180° rotation about the vertical axis in respect to view in (A) shows more clearly the two stretches of TPX2 binding to Aurora-A. (C) The upstream stretch of TPX2 (red, residues 7–21<sup>TPX</sup>) binds at a hydrophobic surface groove present in the N-terminal lobe of the kinase (gray cartoon, yellow side chains). Details of the extensive interactions are shown in the same orientation as in (B). Aurora-A residues are labeled in black, and TPX2 residue labels are color coded as the structure. (D) The downstream helical stretch of TPX2 (pink, residues 30–43<sup>TPX</sup>) binds Aurora-A near helix αC and the activation segment, close to but not directly in contact with phospho-Thr288<sup>AUR</sup> (green). Details of interactions are shown in the same orientation as in (B) and (C).

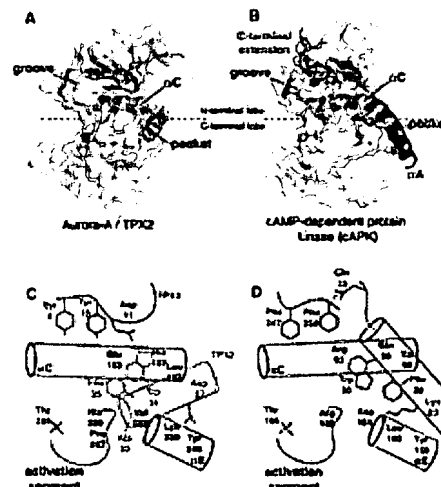


Figure 5.

Figure 5. TPX2-Aurora-A Intermolecular Interactions Resemble cAPK Interactions (A and B) Transparent surfaces representing the conserved cores of (A) Aurora-A and (B) cAPK show similar surface grooves in lobe (between helix αC and the β sheet, gray cartoon) and a similar the two lobes (formed by the activation segment and helix αC, gray portions of TPX2 binding to Aurora-A are shown in red and pink (A), C-terminal extensions to the cAPK catalytic core are shown in light I (D) Schematic diagram of the intermolecular interactions between Aurora-A TPX2 (pink and red) and of the cAPK intramolecular interactions (ligand) that their mode of recognition at the atomic level is rather similar. The interactions of Tyr8<sup>TPX</sup>, Tyr10<sup>TPX</sup>, Trp34<sup>TPX</sup>, and Phe35<sup>TPX</sup> recapitulated by Phe347<sup>cAPK</sup>, Phe350<sup>cAPK</sup>, Trp30<sup>cAPK</sup>, and F

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